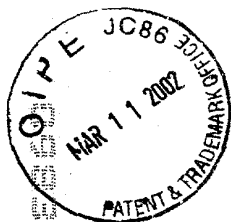


# 9

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: SIFFERT, W.                      Group:              Not yet assigned  
Application No.: 09/836,697                      Examiner:              Not yet assigned  
Filed: 04/16/2001  
(Continuation of 09/180,783 – Filed: 17 March 1999)  
For: THE USE OF A GENETIC MODIFICATION IN THE GENE FOR  
HUMAN G PROTEIN  $\beta_3$  SUBUNIT FOR THE DIAGNOSIS OF  
DISEASES



CERTIFICATE OF MAILING (37 C.F.R. SECTION 1.8(a))

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Date 2/28/2002                      Nicole M. Signac  
(type or print name of person mailing paper)

Nicole M. Signac  
Signature of person mailing paper

Assistant Commissioner for Patents  
Washington D.C. 20231

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SECOND PRELIMINARY AMENDMENT

Preliminary to calculation of the filing fee and examination on the merits, please amend the application identified in caption as follows:

IN THE CLAIMS:

Please amend claims 13, 15 and 20 and add new claims 32 - 36 as follows:

13. A method of diagnosing a disease in a human subject comprising determining the presence of a genetic modification in a gene obtained from the subject which encodes a human G protein  $\beta_3$  subunit.
15. The method as claimed in Claim 13, wherein said gene which encodes a human G protein  $\beta_3$  subunit has the nucleotide sequence of SEQ ID NO: 1.
20. A method for establishing the relative risk of developing a disorder associated with G protein dysregulation in a human subject, the method comprising the steps of:

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- (i) determining the presence of a genetic modification in a gene obtained from [a] the subject which encodes a human G protein  $\beta_3$  subunit;
- (ii) in the event the presence of a genetic modification is determined, assigning the subject an increased risk of disease.

32. A method of diagnosing a disorder associated with G protein dysregulation, said method comprising:

- (i) obtaining from a subject a gene which encodes a human G protein  $\beta_3$  subunit;
- (ii) determining the presence of a genetic modification in said gene from the nucleotide sequence of SEQ ID NO: 1; and
- (iii) associating said genetic modification with said disorder.

33. The method as claimed in Claim 32 wherein said disorder is selected from the group consisting of cardiovascular disease, a metabolic disturbance, and an immunological disease.

34. The method as claimed in Claim 32 wherein said genetic modification in said gene is a substitution for cytosine by thymine at position 825 in SEQ ID NO: 1.

35. The method as claimed in Claim 32 wherein said subject is a human subject.

36. A method for diagnosing an increased likelihood of hypertension in a human subject comprising determining the presence of a genetic modification in a gene obtained from said subject which encodes a human G protein  $\beta_3$  subunit by comparing said gene to the gene sequence of SEQ ID NO: 1, wherein said genetic modification is a substitution of cytosine by thymine at position 825 in SEQ ID NO: 1, wherein the presence of said genetic modification is associated with an increased likelihood of hypertension.

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### REMARKS

By the present Preliminary Amendment, Applicants have amended claims 13, 15 and 20 and added new claims 31 - 36. No new matter has been added by virtue of the amended claims and their entry is respectfully requested.

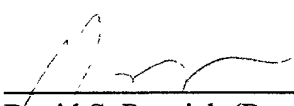
In the event that there are any questions relating to this Amendment or to the application in general, it would be appreciated if the Examiner would contact the undersigned attorney concerning such questions so that prosecution of this application can be expedited.

Entry of the foregoing and prompt and favorable consideration of the subject application on the merits are respectfully requested.

Date: \_\_\_\_\_

Respectfully submitted,

Customer No.: 26770

  
\_\_\_\_\_  
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**VERSION WITH MARKINGS TO SHOW CHANGES MADE IN CLAIMS**

13. (AMENDED) A method of diagnosing a disease in a human subject comprising determining the presence of a genetic modification in a gene obtained from [a] the subject which encodes a human G protein  $\beta_3$  subunit.
14. The method as claimed in Claim 13, wherein said disease is a disorder associated with G protein dysregulation.
15. (AMENDED) The method as claimed in Claim 13, wherein said gene which encodes a human G protein  $\beta_3$  subunit [is the gene] has the nucleotide sequence of SEQ ID NO: 1.
16. The method as claimed in Claim 15, wherein the genetic modification is in the codon for amino acid 275 in SEQ ID NO: 1.
17. The method as claimed in Claim 16, wherein the genetic modification is a substitution of cytosine by thymine at position 825 in SEQ ID NO: 1.
18. The method as claimed in Claim 14, wherein the disorder is a cardiovascular disease, a metabolic disturbance or an immunological disease.
19. The method as claimed in Claim 14, wherein the disorder is hypertension.
20. (AMENDED) A method for establishing the relative risk of developing a disorder associated with G protein dysregulation [for a] in a human subject, the method comprising the steps of:
  - [(I)] (i) determining the presence of a genetic modification in a gene obtained from [a] the subject which encodes a human G protein  $\beta_3$  subunit;
  - [(II)] (ii) in the event the presence of a genetic modification is determined, assigning the subject an increased risk of disease.

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21. The method as claimed in Claim 20, comprising comparing said gene obtained from a subject which encodes a human G protein  $\beta_3$  subunit to the gene sequence of SEQ ID NO: 1.
22. The method as claimed in Claim 21, wherein the genetic modification which is determined is the presence of a thymine (T) at position 825 in the gene obtained from the subject.
23. The method as claimed in Claim 20, wherein the presence of a genetic modification in the gene obtained from a subject is determined by sequencing.
24. The method as claimed in Claim 23, further comprising the step of amplifying the gene obtained from the subject before sequencing.
25. The method as claimed in Claim 23, wherein a section the gene from the host corresponding to position 825 in the gene of SEQ ID NO: 1 is amplified.
26. The method as claimed in Claim 20, wherein the presence of a genetic modification in the gene obtained from the subject is determined by hybridization.
27. The method as claimed in Claim 20, wherein the presence of a genetic modification in the gene obtained from the subject is determined by cleavage using a restriction enzyme.
28. The method as claimed in Claim 27, wherein the restriction enzyme is Dsa I.
29. A non-human transgenic animal comprising a gene which encodes a modified human G protein  $\beta_3$  subunit.
30. The non-human transgenic animal as claimed in Claim 29, which encodes a modified human G protein  $\beta_3$  subunit of SEQ ID NO: 1.
31. The non-human transgenic animal as claimed in Claim 30, wherein said modified human G protein  $\beta_3$  subunit includes a substitution of cytosine with thymine at position 825.

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32. (NEW) A method of diagnosing a disorder associated with G protein dysregulation, said method comprising:
- (i) obtaining from a subject a gene which encodes a human G protein  $\beta_3$  subunit;
  - (ii) determining the presence of a genetic modification in said gene from the nucleotide sequence of SEQ ID NO: 1; and
  - (iii) associating said genetic modification with said disorder.
33. (NEW) The method as claimed in Claim 32 wherein said disorder is selected from the group consisting of cardiovascular disease, a metabolic disturbance, and an immunological disease.
34. (NEW) The method as claimed in Claim 32 wherein said genetic modification in said gene is a substitution for cytosine by thymine at position 825 in SEQ ID NO: 1.
35. (NEW) The method as claimed in Claim 32 wherein said subject is a human subject.
36. (NEW) A method for diagnosing an increased likelihood of hypertension in a human subject comprising determining the presence of a genetic modification in a gene obtained from said subject which encodes a human G protein  $\beta_3$  subunit by comparing said gene to the gene sequence of SEQ ID NO: 1, wherein said genetic modification is a substitution of cytosine by thymine at position 825 in SEQ ID NO: 1, wherein the presence of said genetic modification is associated with an increased likelihood of hypertension.